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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,481	11/30/2001	Francis Barany	19603/3331 (CRF D-2634A)	6387
7590 11/07/2005			EXAMINER	
Michael L. Goldman NIXON PEABODY LLP Clinton Square P.O. Box 31051 Rochester, NY 14603			TUNG, JOYCE	
			ART UNIT	PAPER NUMBER
			I637	
DATE MAILED: 11/07/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,481	BARANY ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41, 46-86 and 155 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-41, 46-86 and 155 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/31/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response filed 8/31/2005 to the Office action has been entered. Claims 1-41, 46-86 and 155 are pending.

1. The rejections of claims 1-41, 46-86 and 155 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in section 2(a) and 2(c) are withdrawn because of the amendment.

2. The rejections of claims 1-41, 46-86 and 155 under 35 U.S.C. 112, second paragraph in section 2(b) is maintained.

a. Claims 1-41, 46-86 and 155 are vague and indefinite because of the phrase “substantially” in claims 1, 17, 46, 62 and 155. It is unclear what is the definition of the phrase in the specification.

The response argues that the term “substantially” in patent claims is well accepted and the meaning of the term would have been clear to one of ordinary skill in the art. The response cited some case law. However, although the use of “substantially” may be appropriate in some cases, each case must be examined on its own merits. It is submitted that in the specific context of the instant claims, “substantially” renders the claims indefinite.

Allowable Subject Matter

3. Claims 1-41, 46-86 and 155 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

4. The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 1-41, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising providing a sample containing normal target nucleotide sequence as well as the mutant nucleic acid sequence, performing polymerase chain reaction on normal target nucleotide sequence as well as the mutant nucleic acid sequence with two labeled oligonucleotide primers, forming heteroduplexed amplified products, nicking or cleaving the heteroduplexes products with an endonuclease which preferentially nicks or cleaves at a location one base away from mismatched base pairs, resealing the nicked heteroduplexed products, separating the products from the ligase resealing reaction mixture by size and detecting the presence of the normal target and the mutant nucleic acid sequence in the sample.

Concerning claims 46-86, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising the different steps compared with claim 1 which are providing a sample potentially containing the mutant nucleic acid sequence but not necessarily the normal target nucleic acid sequence and a standard containing the normal target nucleic acid sequence.

Concerning claim 155, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising the several additional steps compared with claims 1 and 46 which are using polymerase with 3'-5' exonuclease activity to remove several bases 3' to the nick, and using a polymerase without 3'-5' exonuclease activity and labeled dideoxyterminator to perform mini-sequencing reaction and detecting the presence of the normal target and the mutant nucleic acid sequence by mini-sequencing.

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The closest prior art is the reference of Weghorst et al. Weghorst et al. disclose specifically detecting DNA mismatches between heteroduplex strands produced between wildtype and mutation. The method of Weghorst et al. applies the chemical modification of the heteroduplex with reagent that forms a covalent linkage to a mismatched nucleotide in the heteroduplex and detecting the chemically modified mismatched nucleotide. Weghorst et al. do not disclose applying the heteroduplexes, which are nicked or cleaved with endonuclease and resealed with ligase.

Summary

5. No claims are allowable.
6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joyce Tung *J.T.*
October 31, 2005

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

11/2/05